REMARKS

Claims 1-20 are pending in the present application. The Examiner rejects all of the pending claims 1-20.

Objections

The priority claim to the original Canadian patent application is defective as submitted too late in July, 2004. Applicants submit herewith a Petition with the petition fee in order to have it accepted as unintentionally late.

The Oath/Declaration is defective because it does not set forth the claim to priority to the original Canadian patent application. Applicants are awaiting signatures on a corrected and newly signed Oath/Declaration.

The specification is objected to because the priority claim is slightly misstated and should be corrected to indicate that the first United States application in the series was filed pursuant to 35 USC 111. Applicants herein amend the specification to include this reference to the applicable statute.

Claims 8 and 15 are objected to because the steps "a.", etc. are not written as "a)", etc. Applicants herein correct this deficiency.

Rejection under 35 USC 103(a)

DeBaetsalier in view of Winkelhake *et al.*

Claims 1-20 remain rejected under 35 USC Section 103(a) as obvious over US Pat. No. 4,737,455 (to DeBaetsalier) in view of Winkelhake *et al.* (Journal of Infectious Diseases, Vol. 165, pp. 26-33, 1992).

The Examiner previously said that De Baetselier teaches the property of phagocyte cells to show chemiluminescence when activated by certain chemical or immunological agents used for qualitative or quantitative measurement of analytes in biological fluids. Allegedly, a variety of analytes such as endotoxins, lymphokines, membrane specific antibodies and their antigens, toxic substances and others can be analyzed by this method. Moreover, a chemiluminescent substrate such as luminol or lucigenin is added to intensify the chemiluminescence. De Baetselier use hybrid phagocyte cells instead of normal phagocyte cells. The Examiner earlier admitted that ***the methods of De Baetselier differ from those of the present invention in using hybrid phagocyte cells and in using a different control sample, i.e. one without the fluid to be analzyed rather than one without the antibodies against the target antigen.*** However, the Examiner maintained that it would have been obvious to one of ordinary skill in the art to modify the method of DeBaetselier by using the claimed normal phagocyte cells and to modify the control sample by deleting reagent antibody instead of sample fluid in order to control for the variability of the normal phagocyte cells. Additionally, the Examiner said that De Baetselier teaches that the amount of chemiluminescence is proportional to the amount of stimulator/analyte/antigen present. The Examiner further admitted that ***De Baetselier do not teach detecting gram negative bacteria*** such as *E. coli, Klebsiella pneumoniae* or *Pseudomonas aeruginosa.* However, the Examiner said that it was routine to detect gram negative bacteria for diagnosing sepsis and infection using antigen-antibody interactions and cites to Winkelhake *et al.* as teaching gram negative bacteria.

The legal test for *prima facie* obviousness

As the Examiner knows, in order to establish a proper *prima facie* case of obviousness, the Examiner must establish that there is a suggestion or motivation to modify the references or to combine the reference teachings; there must be a reasonable expectation of success; and the references or combination of references must teach or suggest all of the claim limitations (*see, e.g.,* MPEP § 2142). The teachings or suggestions to make the claimed combination and the reasonable expectation of success must both be found in the prior art and not based on applicant's

disclosure (*In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cr. 1991)). The arguments advanced by the Examiner fail to meet all of these criteria.

De Baetselier does not teach or suggest the present invention alone or in combination

De Baetselier do not teach or suggest many facets of the instant invention. The presently claimed method employs a measure of oxidants produced by white blood cells present in a reaction in the determination of the quantity of an analyte from a comparison of the oxidant produced by white blood cells. No standard curve relating direct assay readout to analyte level is employed as in the prior art, as this would require a standard curve for every test. In contrast, the present invention is based on a highly reproducible relationship between the amount of oxidant produced by white blood cells and the amount of analyte in the sample, as noted on page 20, lines 17-20 and page 21, lines 1-4. Hence, the amount of analyte may be quantitated from this single determination.

Moreover, the methods according to the presently claimed invention may be carried out with white blood cells endogenously present in the sample or from another source or sources, and do not require the addition of hybrid cells as required by the methods of De Baetselier. It is simply unnecessary to add a standardized white cell population in the presently claimed methods. Applicants have discovered that unstandardized endogenous white blood cells are sufficient to provide a quantitative test. Applicants note that the present invention is not limited by the source of white blood cells which may include any combination of those endogenously present in the sample, as well as added cells from another source or, indeed, hybrid cells. However, Applicants reiterate that De Baetselier does not teach or suggest using a single quantification of oxidants rather than a standard curve, regardless of the source of white blood cells, to provide a quantitative readout. Applicants provide methods that make this possible, representing a significant and unobvious advancement over the prior art.

Winkelhake *et al.* do not cure the deficiencies of De Baetselier

The Examiner cites to Winkelhake *et al.* as teaching that gram negative bacteria may be detected using an antigen-antibody interaction and thereby used to diagnose infection and sepsis. Applicants do not dispute the fact that detecting gram negative bacteria is clinically useful. The present invention is not novel and nonobvious over the prior art methods because it may be applied to detecting gram negative bacteria. Rather, the present invention is novel and nonobvious because of the manner in which such detection is performed. Hence, Winkelhake *et al.* in no way cure the deficiencies of De Baetselier. As such, the very first part of the test of *prima facie* obviousness goes unmet.

Lilius *et al.*

The Examiner makes a new rejection of claims 1, 2, 5, 6, 8, 9, 12, 14, 15, 18, and 20 under 35 USC 103(a) over Lilius *et al.* (Journal of Bioluminescence and Chemiluminescence 7:117-122, 1992). According to the Examiner, it would have been *prima facie* obvious to one of ordinary skill in the art to alternatively detect the antigen in a sample of a body fluid such as serum by contacting with the cognate antibody because Lilius *et al.* specifically teach that the amount of antigen can be measured.

Applicants respectfully disagree. There is simply no reasonable expectation of successfully detecting the antigen in a sample of a body fluid such as serum by contacting with the cognate antibody because Lilius *et al.* A motivation to make the change and a reasonable expectation in succeeding are required in order for a rejection under 35 USC 103 to be proper.

Lilius *et al.* in view of Winkelhake *et al.*

The Examiner makes a second new rejection of claims 1-20 under 35 USC 103(a) over Lilius *et al.* (Journal of Bioluminescence and Chemiluminescence 7:117-122, 1992) in view of Winkelhake *et al.* (Journal of Infectious Diseases, Vol. 165, pp. 26-33, 1992). ***According to the Examiner, it would have been prima facie obvious to one of ordinary skill in the art to modify***

the assay of Lilius et al. to use a whole blood sample comprising both analyte and leukocytes in the chemiluminescent assay because Winkelhake *et al.* teach that whole blood leukocytes are functional in a luminal dependent chemiluminescent assay. Also, the use of leukocytes from a sample of whole blood would reduce the number of steps required to perform the assay.

As the Examiner knows, in order to establish a proper *prima facie* case of obviousness, the Examiner must establish that there is a suggestion or motivation to modify the references or to combine the reference teachings; there must be a reasonable expectation of success; and the references or combination of references must teach or suggest all of the claim limitations (*see, e.g.,* MPEP § 2142). The teachings or suggestions to make the claimed combination and the reasonable expectation of success must both be found in the prior art and not based on applicant's disclosure (*In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cr. 1991)). The arguments advanced by the Examiner fail to meet all of these criteria. There simply is no motivation within the references to modify the assay of Lilius *et al.* to use a whole blood sample comprising both analyte and leukocytes in the chemiluminescent assay. Moreover, there is no reasonable expectation of success in doing so. Therefore, the rejection does not constitute a proper *prima facie* case of obviousness for these reasons alone.

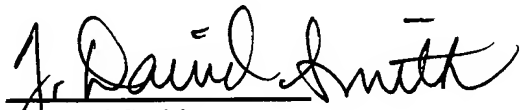
Fees

No additional fees are believed necessary in connection with this submission. However, should this be in error, authorization is hereby given to charge Deposit Account No. 11-1153 for any underpayment, or to credit any overpayments.

Conclusion

Applicants respectfully request entry of the foregoing amendments and remarks. Reconsideration and withdrawal of all of the outstanding rejections is believed in order. Early and favorable action on the claims is earnestly solicited. Should a discussion be helpful in resolving any outstanding issues, the Examiner is invited to telephone the undersigned at (201) 487-5800.

Respectfully submitted,



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